Dr. Koert Gerzon Organic Chemical Division The Lilly Research Laboratories Indianapolis 6, Indiana

Dear Koert:

Yes, I did talk to Dr. Aronow and was encouraged to hear of his tentative findings. I was also glad to learn that his MP resistant cell line is also resistant to the MP riboside, so that the possible sensitivity to the ribotide amidate is less likely to have a trivial explanation of previous hydrolysis to the riboside.

I would indeed be delighted to see some more of the thymidylic acid derivative, thought I hope you may now be prepared to consider synthesizing it with a tritium or C-14 label to allow for a more direct test of its metabolic properties. We have had considerable discussion about this general problem at the institute, and while there is some controversy just how far we should go in this direction, there is pretty general agreement that syntheses with at least moderate levels of labelling ought to be thought of more often! than is usually the case. Unless you feel that it is climbing too far over in samebody else's territory, I would also like to suggest that you consider preparing the corresponding derivatives from fluorouracil, since we have recently started an explicit program of studies on the enzymetic basis of resistance to fu and its riboside and deogyriboside. In addition to the availability of the thymidylic amidate for the nutrition of a thymine mutant, I would also test it for its capacity to reverse the inhibition of E. coll by fluorouracil and its derivatives. We will be checking out the thymine requiring strains and will send them on to you after having done this.

Unfortunately, it is working out, as I had feared it might, that I will be tied down in Baltimore and Washington over the interval that I had hoped I might join the other people from the institute when they visited you. However, I am very pleased that our colleagues will be visiting your laboratories and I am very sure that this will be a useful basis for further communication.

Cordially,

Joshua Lederberg Professor of Genetics